UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte GEORGE JACKOWSKI and JOHN MARSHALL

Appeal 2007-3735
Application 09/993,344
Technology Center 1600

Decided: December 13, 2007

Before DEMETRA J. MILLS, LORA M. GREEN, and NANCY J. LINCK, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal[1] under 35 U.S.C. § 134 from the Examiner's final rejection of claim 1. We have jurisdiction under 35 U.S.C. § 6(b). The claim reads as follows:

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[1] This Appeal is related to Appeal Nos. 2007-3904, USSN 09/991,796, and 2007-3905, USSN 09/991,799, which are decided concurrently with this Appeal.

1. An isolated biopolymer marker consisting of amino acid residues 2-18 of SEQ ID NO: 1 which evidences a link to Alzheimer's disease.

We reverse the rejections of record, but raise other issues that the Examiner should consider upon return of the administrative file.

BACKGROUND

According to the Specification:

> This invention relates to the field of characterizing the existence of a disease state; particularly to the utilization of mass spectrometry to elucidate particular biopolymer markers indicative or predictive of a particular disease state, and most particularly to specific biopolymer markers whose up-regulation, down-regulation, or relative presence in disease vs. normal states has been determined to be useful in disease state assessment and therapeutic target recognition, development and validation.

(Specification 1.)

Proteins are collected from an individual, usually from a serum sample (Br. 11), and are resolved using polyacrylamide gel electrophoresis (Specification 38). The protein bands are cut from the gel, and are cleaved into fragments using proteolytic enzymes (Specification 38). The peptides are collected and purified, and then subject to identification by mass spectrometry (Specification 38-39; Br. 12).

The Specification teaches further:

> The human genome contains the genes that encode all proteins. The proteolytic cut sites within all these proteins can be predicted from the translated amino acid sequence. The mass of the peptides that result from the predicting cut sites can be calculated. Similarly, the fragmentation pattern from each hypothetical peptide can be predicted. Thus, we can

> conceptually digest the proteins within the human proteome and fragment them.
>
> When a peptide has been "sequenced" it is understood that the peptide fragment has been purified by one of the methods above, i.e. Time of flight (TOF) or by chromatography, before fragmenting it with gas to produce the peptide fragments. The original peptide mass and fragmentation pattern obtained is then fit to those from the theoretical digestion and fragmentation of the genome. The peptide that best matches the theoretical peptides and fragments and is biologically possible, i.e. a potential human blood-borne protein, is thus identified. It is possible to identify plural targets in this fashion.

(Specification 39-40.)

As to the peptide of SEQ ID NO:1, the Specification teaches:

> As a result of these procedures, the disease specific markers (J02908) apolipoprotein J precursor having a molecular weight of about 1873.9911 daltons and a sequence of SEQ ID NO:l; (M74816) sulfated glycoprotein-2 having a molecular weight of about 1873.9911 daltons and a sequence of SEQ ID NO:2; and (J02908) apolipoprotein J precursor having a molecular weight of about 1393.6963 daltons and a sequence of SEQ ID NO:3 related to [sic. Alzheimer's] disease were found.

(Specification 46, as amended June 9, 2003.)

DISCUSSION

Claim 1 stands rejected under 35 U.S.C. § 101 "because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility or a well established utility." (Answer 3.)

The rejection of the peptide of claim 1 is predicated on the argument that the Specification does not disclose whether the fragment is "present, not present or present at different levels in samples identified as obtained from

AD [Alzheimer's disease] patients" (*id.* at 5), and thus the Specification has not established the utility of the peptide as a biomarker for Alzheimer's disease (*id.* at 3-8).

As acknowledged by the Examiner, the Specification teaches that the peptide of SEQ ID NO:1 is a fragment of apoliporotein J precursor protein (*id.* at 4). Thus, if we take a step back and look at the subject matter of the claim, at bottom, claim 1 is limited to a peptide fragment of a known protein, apolipoprotein J. Apoliprotein J, also known as clusterin and sulfated glycoprotein 2, has been implicated in the pathogenesis of Alzheimer's disease (Lidström,[2] p. 435). As noted by Lidström, antibodies to clusterin label senile plaques and neurofibrillary tangles (*id.*).

Thus, peptide fragments derived from apoliporotein J would have the well established utility as antigens for the generation of antibodies which can be used to localize or assay for the protein. We note in addition that the Specification also discloses that antibodies may be raised to the markers disclosed by the invention (Specification 49-52). Thus, as we conclude that the peptide of SEQ ID NO:1 would have the well established utility of generating antibodies specific for apolipoprotein J, we are compelled to reverse the rejection.

The Examiner also rejected claim 1 under 35 U.S.C. § 112, first paragraph, on the grounds that "since the claimed invention is not supported by either a clear asserted utility or a well established utility . . . one skilled in

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[2] Lidström *et al.*, "Normal levels in clusterin in cerebrospinal fluid in Alzheimer's disease, and no change after acute ischemic stroke," *Journal of Alzheimer's disease*, Vol. 3, pp. 435-442 (2001) (submitted in the IDS of July 7, 2003).

the art clearly would not know how to use the claimed invention." (Answer 8.) This rejection is also reversed for the reasons set forth above.

OTHER ISSUES

Upon return of the administrative file, the Examiner should reevaluate the patentability of the claim in view of the prior art.

As acknowledged in the Specification, SEQ ID NO: 1 is a fragment of apolipoprotein J precursor (Specification 49). Moreover, the Specification teaches that specific sequences were determined as a fit to those from the theoretical digestion and fragmentation of the genome (Specification 39-40). Thus, SEQ ID NO:1 is a trypsin fragment of a known protein sequence.

In that regard, we cite Kapron,[3] which teaches a peptide of SEQ ID NO: 2 (p. 2126, Table 4, residues 182-198). The peptide disclosed by Kapron is as fragment of clusterin produced by digestion with trypsin (abstract) identified by liquid chromatography electrospray mass spectrometry (Table 4). Note that SEQ ID NO. 2 has the same mass of SEQ ID NO: 1 (Specification 49), and only differs from SEQ ID NO: 2 in residues 4-6. In SEQ ID NO: 1, residues 4-6 are SDS, while in SEQ ID NO: 2, the residues are DSD. However, given the method of sequencing laid out in the Specification and discussed above, the sequence of the peptide of SEQ ID NO:1 must be derived from a known sequence of apolipoprotein J precursor.

[3] Kapron *et al.*, "Identification and characterization of glycosylation sites in human serum clusterin," *Protein Science*, Vol. 6, pp. 2120-2133 (1997), a copy of which is included with this opinion .

CONCLUSION

In summary, we reverse the rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, first paragraph, but raise other issues as to the patentability of claim 1 that the Examiner may wish to address upon receipt of the administrative file.

REVERSED

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MCHALE & SLAVIN, P.A.
2855 PGA BLVD
PALM BEACH GARDENS FL 33410